How To Practice Like An Internist

"Liquid Biopsy" for Cancer Detection

Cancer is the leading cause of dogs over the age of 1. We all see it nearly every week in most of our practices. Everyone is looking for a way to prevent it. If we can't prevent it, then we want to diagnose it early, accurately, "minimally-invasively", inexpensively, efficiently. Unfortunately, our options in the past have been somewhat limited. Physical exam and minimum database are just not sensitive enough to detect cancer early in many of our patients. As a result, we are often put into a reactive position, where a client brings their pet in because they are showing significant signs of illness and then we try to find the cancer. We would love to find cancer BEFORE it causes serious problems.

Recent technology has resulted in the development of "liquid biopsy" tests for use in dogs. The purpose of these tests is to detect cancer earlier in the disease process and to use them for the screening of at-risk breeds prior to the presence of clinical signs. They are also being used to aid in the diagnosis of cancer in pets where cancer is strongly suspected, but not easily found using routine diagnostic tools or when the suspected cancer site cannot be easily accessed to obtain biopsies.

There are at least two liquid biopsy tests on the market at this time, the OncoK9 test and the Nu.Q. Vet Cancer Test. I have only used the OncoK9 test thus far, so the specifics that I will be talking about today are based on THAT test, but both use the same general concept to try to detect cancer in dogs. Each has its own protocol for obtaining samples and preparing the samples for evaluation. Each has pros and cons. Each has their own limitations. Neither test is appropriate for use in our feline patients.

Cancer is caused by abnormal changes in the the DNA of a patient. When cells die in the body, whether they are normal cells or cancer cells, they release their contents into the bloodstream. One component of the cell content that is released is cell-free DNA. The OncoK9 test uses a process, termed Next-Generation Sequencing, to detect specific abnormalities in the cell-free DNA released from cancer cells. When these abnormalities are detected, we know that cancer is present in that patient.

Studies have shown that the OncoK9 test is able to detect up to 30 different types of cancer in dogs. The three most aggressive tumors affecting dogs include lymphoma, hemangiosarcoma and osteosarcoma. The OncoK9 test has a detection rate of 85% for those three tumor types. Eight of the most common tumor types in dogs include: lymphoma, osteosarcoma, hemangiosarcoma, anal gland adenocarcinoma, mast cell tumor, melanoma, soft tissue sarcoma and mammary gland adenocarcinoma. The OncoK9 test has an overall detection rate of 62% when all of those tumors are considered as a group.

Is this test good for every type of cancer? Definitely not. Some tumor types are difficult to detect with the liquid biopsy. These tumor groups include neoplasia of the CNS, the urinary tract, the nasal cavity and focal tumors of the skin. While the OncoK9 test COULD possibly detect cancer signs in those cases, the detection rate is much lower for those and a negative test result would not completely rule-out the presence of cancer.

So, what can you expect with the results of the OncoK9 test? It will give the practitioner a result of either "Cancer Signal Detected" or "Cancer Signal Not Detected". The false positive rate for

all cancers detected was 1.5% and the overall specificity of the test is 98.5%. So, if you get a positive result, you can be quite confident that cancer is present in your patient. If you get a negative result, then you need to continue your work-up and know that, while cancer is not as likely, it could possibly still be present in that patient. As with many diagnostic tests, the result should be taken in context with the signalment, clinical signs, clinical suspicions and should never be used as the sole source for clinical decision making.

So, how should this test be used? It has really been marketed as a tool for early cancer detection in dogs. As a screening tool, it could be used in cases of middle-aged to older pets that are not showing any clinical signs of cancer but are of a breed that is prone to developing cancer such as Golden Retrievers, Rottweilers, Boxers, Bernese Mountain Dogs and French Bulldogs. The goal would be to try to detect the presence of cancer prior to signs of illness.Pets would be expected to have a better long-term prognosis if we could begin treatment earlier in the course of disease.

When the test is being used as a screening test for an apparently healthy dog with no sign of cancer and the Cancer Signal Detected result is obtained, there is a 76-80% chance that the patient HAS cancer and further diagnostics would be warranted to try to find out where it is and what it is. When used as a screening test in an apparently healthy dog and there is no cancer signal detected, there is a 95-96% chance that the dog does not have cancer.

The OncoK9 test can also be used as an aid in the diagnosis of cancer. I tend to use this test when my initial diagnostics are suggestive of cancer, but more invasive testing would be required to obtain a definitive diagnosis. For instance, an older dog with a ruptured spleen tumor that was detected with ultrasound. We know that many of these cases are hemangiosarcoma. The only way to obtain a definitive diagnosis is to obtain a biopsy of the spleen tumor, which would involve exploratory laparotomy. In some cases, clients would be more likely to pursue surgery to remove a benign spleen tumor, which would carry a good long-term prognosis, compared to pursuing surgery to remove hemangiosarcoma, which would typically carry a very poor long-term prognosis. If we had a minimally invasive way to get this information, who wouldn't want that? The OncoK9 test could be used to help us make our decision. Remember, hemangiosarcoma is one of the cancer types that the OncoK9 test can detect quite reliably.

When the test is being used as an "Aid in Diagnosis" for a pet that is showing signs of cancer and a cancer signal is detected, there is a 94-97% chance that the patient has cancer. When used as an aid in the diagnosis of a pet that is suspected to have cancer and there is no cancer signal detected, there is a 68-84% chance that cancer is not the cause of the dog's illness.

Is this a perfect test? Absolutely not. Does it have the potential to diagnose pets with cancer earlier, before they show signs of illness? Absolutely. Could it be another tool in our toolbox to help us make better diagnostic and treatment recommendations for our clients to help care for their pets? Absolutely.

Bexacat

This product is an oral hypoglycemic medication for cats, called Bexacat, marketed by Elanco. It was just made available to general practitioners in March of this year. Traditionally, our treatment regimen for diabetic cats included insulin injections twice daily and sometimes a diet change to a low carb, high protein diet. Unfortunately, this treatment regimen leaves much to be

desired. A recent study that surveyed pet owners and veterinarians showed that 30% of diabetic cats were euthanized within the first year of treatment, with 2 out of 10 being euthanized at the time of diagnosis. There are so many factors involved in the euthanasia decision, but twice daily insulin injections were a very common denominator.

Bexacat, or bexagliflozin, is a class of drug that has been available on the human side for many years (Jardiance and Brenzavvy). It is now being used as a treatment for diabetes in cats. It is a sodium-glucose cotransport (SGLT-2) inhibitor. SGLTs play an important role in maintaining glucose balance in the blood.

Let's talk briefly about the concept behind this drug. The kidneys normally filter out quite a bit of glucose. There are SGLT-2 receptors in the kidneys that exist to reabsorb glucose from the glomerular filtrate back into the bloodstream. These receptors are responsible for reabsorbing about 90% of the glucose from the glomerular filtrate back into the blood.

This drug blocks the SGLT-2 receptors, which means that instead of being reabsorbed, most of the glucose passes out of the kidneys into the urine. This results in glucosuria and a lower blood glucose level.

There are also SGLT receptors in the intestinal tract, but they are SGLT-1 receptors. Bexacat does not inhibit those receptors, so some glucose will still be reabsorbed. There is enough glucose reabsorption by those receptors to maintain a normal blood glucose level.

The beauty of this product is that it works quickly, often normalizing blood glucose levels within 7 days. Elanco studies showed that 83% of cats were considered a "treatment success" at Day 56.

What's the catch? What do we need to know? What do we need to be careful with? The catch is that all this drug is doing is creating lower blood glucose. The cat still needs to produce insulin to transport glucose into the cells for normal life functions. So, this is the primary reason why it is only appropriate for use in CATS, because cats are often type-2 or non-insulin dependent diabetics. Dogs are almost always Type-1 or insulin dependent at the time of diagnosis.

I don't think I really understood this as a new veterinarian. I also think that we were figuring this out not too many years ago. Remember, most newly diagnosed diabetic cats still have functional beta cells in their pancreas, so they can still make insulin. When they are diagnosed, they have glucose toxicity which basically burns out the beta cells. If we can decrease the blood glucose sooner, then we can reduce glucose toxicity to the beta cells, allowing them to recover and start making insulin again. That is the main reason that diet change or weight loss is often recommended for diabetic cats to try to reduce one cause of insulin resistance. In some cats, they start off on insulin therapy and later no longer need it. If the beta cells are shot, and the cat can't make insulin, then Bexacat won't work.

So, the current recommendation is that Bexacat is only to be used in cats that have NOT received insulin previously. It is to be used in non-sick, newly diagnosed diabetic cats because these cats have the best chance of being able to produce and respond to their own insulin if we can just get the blood glucose level down for a while to allow the beta cells to recover.

Another big concern is that these Bexacat-treated cats could still develop diabetic ketoacidosis and become very sick. If this happens, and the practitioner doesn't know the cat is on Bexacat

or isn't familiar with the way this product works, they may not recognize it as DKA. This is because the serum glucose level will NOT be markedly increased. Why not? Because the glucose is all being excreted through the urine. But the cat can't utilize the glucose in the blood stream, because they are not producing insulin. So, the first dilemma is making the correct diagnosis, then the second dilemma comes in trying to wrap your head around treating a euglycemic patient with insulin, just as you would a "normal" DKA.

It is impossible to know which cats are still able to produce enough of their own insulin to do well with Bexacat. That is why Elanco is making very strong recommendations for screening patients before starting the product and requiring rechecks during the first few weeks of treatment. Studies have suggested that if a cat is going to have trouble with Bexacat, it is usually within the first 2 weeks of treatment. Some of the screening and follow-up involves measuring fructosamine levels, performing glucose curves, screening for concurrent illnesses, such as pancreatitis, and measuring serum ketone levels using a special ketone monitor, which is very different from measuring ketones in the urine like we are all used to doing. ****The specific recommendations for screening, monitoring and managing cats using Bexacat can be obtained from your Elanco Rep. If you are interested in using this product, I highly recommend that you watch some of the informational webinars from Elanco before using it on one of your patients.**

Less serious side effects from Bexacat could include soft stools or diarrhea, but this is usually self-limiting. Vomiting is always a possible side effect in an oral medication given to a cat. Pancreatitis was also reported. Surprisingly, the incidence of UTI is not any higher in a cat being given Bexacat compared to a normal diabetic cat. Decreased appetite, lethargy and dehydration could all be additional potential side effects.

This drug should be only started on a naive diabetic cat that has no signs of illness, other than what would be expected in a newly diagnosed diabetic - PU/PD, polyphagia, weight loss. The cat needs to be at least 3 kg or 6.6#. If they are ill, not eating, have been diagnosed with pancreatitis at the same time, have untreated hyperthyroidism, etc. it is not recommended to begin treatment with Bexacat.

Bexacat comes in a 15-mg chewable tablet that is quite palatable. It is a one-size-fits-all dose and should be given once daily, at the same time each day. It can be given with or without food. About 20-30% of cats may have persistent PU/PD and polyphagia may persist in 80% of cats, even if they are considered treatment successes.

Histoplasmosis Testing

Histoplasmosis is a common infectious disease in our area. It can be found almost anywhere in the US but is much more common east of the Rocky Mountains. Miravista laboratory, the leader in fungal disease testing, states that "the highest incidence of veterinary cases of histoplasmosis appears to be in Texas and Oklahoma." It exists in the soil as a mold and is most commonly found in the dust of soils that are contaminated with bird and bat droppings. The pet (dogs or cats) inhales the spores and then becomes infected. Cats are affected about 4 times more often than dogs. Interestingly, strictly indoor cats can become infected with histoplasmosis. It is not contagious from pet to pet or pet to person.

The distribution of disease varies, but the lungs are the most common site for cats. It can also involve the liver, kidney, eyes, bone marrow, skin, bones or joints and the intestines. The same

holds true for dogs, but in dogs, the intestinal tract - specifically the colon, tends to be the most affected site.

Practicing in Southern Oklahoma, I usually have histoplasmosis on my differential list for almost any chronically sick cat that I see, regardless of clinical signs, laboratory findings, signalment, etc. It can look like or do just about anything, so don't forget about it.

In the past, we used to use antibody testing, but this is not the most accurate way to diagnose the disease. The histoplasmosis antigen test is currently the best minimally invasive diagnostic tool for diagnosing histoplasmosis. It has a sensitivity rate of 94.4% in cats when urine is submitted as the sole sample source and a slightly lower specificity rate in dogs. Blood or CSF could also be used, but the test is most accurate when performed on urine.

You will often see at reference labs a "fungal panel" that can include histoplasmosis. This is an antibody test that has a sensitivity of <25%, so if you are trying to determine if the pet may have histoplasmosis, that fungal antibody test is not recommended. There is an antibody test available from MiraVista Labs but it is typically only used for the very rare cases where the Histoplasmosis antigen test is negative and Histo is still strongly suspected. In 4-5% of cases, you can have a negative Ag test and a positive Ab test.

The test is obviously critical for making the initial diagnosis of histoplasmosis. When you receive the test result, it will tell you if the pet is positive or negative. If positive, you will also see a quantitative result. This is helpful as you monitor response to treatment. I typically recheck the test 3-4 months after treatment is initiated. If the result is positive, but the value is lower, then treatment is continued for another 3-4 months. Once the test is negative, then treatment can be discontinued. We often recheck the Ag test again in 6 months, then at least yearly, or any time the pet is showing signs of illness that could be consistent with histoplasmosis.

Hydrolyzed Protein diets

This may be too easy or too basic of a topic, but I feel that food trials are under-utilized in dogs and cats with chronic gastrointestinal signs. Research suggests that "food-responsive" enteropathies are the most common chronic enteropathies in dogs. I have had success using hydrolyzed protein diets in pets with chronic vomiting, chronic diarrhea, poor appetite, bad gas, chronic pruritus, recurrent otitis externa, among many others,

What is so special about hydrolyzed protein diets? The hydrolyzation process basically changes the molecular structure of dietary ingredients, making them unrecognizable to the body. Essentially, the body doesn't know that it is eating chicken, for instance. If the body can't recognize the ingredient that it really is, then it doesn't react negatively to it.

The first key to a food trial is to determine if your client is even capable of doing this. Some clients are just not able to stick to a restricted diet, even for a short period of time. Some clients have little kids who don't understand why they can't give their dog some of the food that they are eating, or they may drop it from the table by accident. Some clients with multiple pets are unable or unwilling to keep this pet from getting the food that the others are eating. Some clients don't feed dog food at all. These dogs are almost certainly not going to eat our hydrolyzed protein diets!

Second, you must nicely and tactfully beat it into their heads that NO OTHER food can be given during the trial period. I can't tell you how many people think they are doing the food trial and seem to listen and understand, but don't realize that giving their meds in peanut butter or cheese or giving them boiled chicken as a topper can totally negate what we are trying to do. I try to offer them acceptable alternatives for treats and snacks, which can include prescription treats. Bananas, carrots, cucumbers, apples, ice cubes are all some acceptable, easy treat options that won't affect the food trial.

There are several different options for hydrolyzed protein diets for both dogs and cats. Each of the main pet food manufacturers has their own version of this, my personal preference is Royal Canin hydrolyzed protein diet (HP). I have also started using the Blue Buffalo veterinary formula, which is called HF, just to give clients another option. Hill's makes Z/D and Purina has HA.

The only brands that I do not recommend are the OTC brands of novel protein diets, at least while we are in the test phase of the trial. There are too many variables that are not controlled in the OTC diets, so if the pet doesn't respond, then you really can't say that it isn't a food allergy/intolerance.

My favorite use of the hydrolyzed protein diet is for chronic vomiting cats. It seems like every client with a cat that vomits frequently thinks that it is because they are eating too fast. While this could possibly be a contributing factor, it is just not typically a scientifically proven cause of chronic vomiting in cats. Many of these cases of young, otherwise healthy cats who have a good appetite, are not losing weight and not having diarrhea have food intolerance. I try to get owners to try a food trial with HP food prior to doing more invasive diagnostics or trying prednisone.

Bladder tumors

Urothelial carcinoma is the most common cause of cancer of the lower urinary system in dogs. Several breeds have a genetic pre-disposition for the development of these tumors, including Scotties, Westies, Beagles and Shelties. Diagnosis of tumors involving the lower urinary tract is often delayed, because clinical signs are typically assumed to be due to a bladder infection initially, as most pets exhibit pollakiuria, stranguria, and at least intermittent hematuria that often seems to improve temporarily while on antibiotics. Unfortunately, because of this, many of these tumors are advanced by the time we diagnose them.

Ultrasound is the most common and widely available diagnostic tool to identify urothelial neoplasia. Masses within the bladder are typically very easy to identify with ultrasound and are most often located near the trigone region of the bladder. When masses are present primarily within the urethra, identification becomes more difficult.

When I am faced with a bladder tumor, I explain to the owner that there is a very high likelihood that the mass is neoplastic. We also discuss the fact that surgical excision of the mass is not typically recommended or often not possible. In the past, options to obtain a definitive diagnosis were quite limited and fairly invasive. Surgical biopsies could be performed, but often are not, because surgical excision was not likely to be curative. As a result, most clients did not want to put their pet through an invasive surgical procedure just to obtain a biopsy. Traumatic catheterization with subsequent cytology was sometimes performed, which often provided diagnostic results. Cytology of a urine specimen sometimes leads to a diagnosis or at least a presumptive diagnosis but can be complicated by inflammation secondary to either tumor or

infection. Percutaneous FNA of a bladder mass is not recommended due to the possibility of seeding cancer cells into the abdomen or SQ tissue along the needle tract.

More recently, there is a test called the urine BRAF test, which can now be used to aid in the diagnosis of urothelial cancer in dogs. Mutations in a gene called BRAF are common in urothelial carcinomas, being present more than 80% of the time. The BRAF test is a PCR based genetic test that evaluates a urine sample for a specific mutation of the canine BRAF gene. The test is performed on a free-catch urine sample and is not affected by hematuria, proteinuria or urinary tract infection. This test is currently only available through ANTECH. There is about a 15% chance of false negatives with this test.

While there are numerous options for the management of lower urinary tract neoplasia in dogs, none are curative. Unfortunately, most pets are euthanized within 6 months of diagnosis due to progression of clinical signs and declining quality of life.

I have used many different chemotherapeutics in my patients, but have found that therapy with the NSAID, piroxicam, often results in the most satisfactory outcomes. The beauty of this treatment is that it is relatively safe, easy, affordable, readily available and you don't need any special equipment to use it in your patients.

Piroxicam is an NSAID that has been shown to have anti-tumor effects. It has been used in human medicine as a chemotherapeutic. Severe side effects are uncommon, but could include GI upset or ulceration, nephrotoxicity or hepatotoxicity. It often relieves the straining and clinical signs associated with urothelial tumors in dogs quite quickly and seems to do so for a significant period in many pets. In many of my patients, I see survival times of 9-12 months or more using piroxicam alone.

The recommended dose is 0.3mg/kg PO SID for dogs. It typically needs to be compounded, because the commercially available capsules are either 10 mg or 20 mg capsules, which would only be appropriate for large dogs.

An additional supplement that I have recently been adding to my urothelial carcinoma management is a supplement marketed by Nutramax. Avmaquin contains a metabolite found in broccoli. Studies over the years have suggested that diets rich in certain vegetables may lower the risk of cancer in people. Sulforaphane is a compound found in some plants that has been identified as a potential chemoprotective agent. It is found in highest concentrations in broccoli. Once it is broken down by the body after ingestion, it is excreted in the urine and some studies have suggested that it may inhibit cancer development in the urinary tract. There is also some thought that it could slow cancer growth. Because it is a nutraceutical, I have decided to start using it in my patients with confirmed or suspected urinary neoplasia and even in a few pets with chronic bladder issues, such as dogs that have had previous surgery for IVDD and no longer have normal urinary function. It may possibly limit inflammation in the bladder, which could be a risk factor for the develoment of neoplasia.

FIP

FIP has long been considered a universally fatal disease in cats. It is difficult to diagnose and is devastating for the owners, as most cats afflicted by FIP are young, usually under the age of 2. We know that most cats have been exposed to coronavirus and have antibodies to the virus. We know that FIP is caused by a mutation of the feline enteric coronavirus. About 1 in 10 cats exposed to the mutant virus will go on to develop FIP.

The classic case of FIP is a male kitten or young adult cat, often from a multi-cat environment such as a feral cat colony, a shelter or cattery. They typically present like most sick cats with decreased appetite, weight loss, lethargy and usually a fever. There are two forms of FIP - the wet form and the dry form. In the wet form, the kitten may have a distended abdomen due to peritoneal effusion or labored breathing because of pleural effusion. The dry form can cause almost any clinical sign.

Although we often have a strong suspicion for FIP in certain cases, there is not currently a reliable ante-mortem test for FIP. Basic lab abnormalities can help confirm a diagnosis of FIP, with hyperglobulinemia being the most consistent finding. A low albumin:globulin ratio (less than 0.9) is suggestive of FIP. Hyperbilirubinemia may or may not be present, but its presence is a poor prognostic indicator. Cats with a t.bili of >4.0 are not likely to survive. In cases of the wet form of FIP, fluid analysis of the effusion can help guide your diagnosis – a high protein level with a low cellularity and an albumin:globulin ratio of less than 0.8 is suspect for FIP. Feline coronavirus serology is NOT HELPFUL and should not be used to diagnose FIP. PCR of effusion or blood could possibly be helpful if it were positive, but may be negative even if FIP is present.

So, what is this talk about a treatment???

There are no FDA-approved drugs for the treatment of FIP. Two targeted antiviral therapies exist that have been used with significant success in cats with FIP. The drugs are GC 376 and GS-441524 (or “GS” for short). GS seems to be more effective and is the parent drug of the more well known anti-viral called remdesivir, which most of us became aware of during the COVID pandemic. Unfortunately, the company that owns the patent for that GS drug has not produced a product approved for use in cats. Because there is not an approved product and because the drug showed so much promise in the treatment of FIP in cats, multiple “black market” manufacturers started producing the drug on their own. The problem is that we know very little about these drugs, they are not FDA-approved, they are changing all the time and the sourcing of these drugs is questionable at best. Additionally, they are typically very expensive, often thousands of dollars for the course of treatment.

So, what can be done to help these cats if there is not an approved product available to veterinarians? Reach out to social media, of course. There is a private Facebook group called FIP Warriors. The group is made up of individuals who help facilitate drug procurement and guide therapy for these cats. There is also an FIP Warriors group for veterinarians.

Even though it is a little bizarre and there are obviously ethical questions that arise, you can’t argue with results. A veterinarian from The Ohio State University performed a study a few years ago surveying 400 cat owners and over 150 vets involved in the FIP Warriors group. The study showed survival rates of over 80% in these FIP cases.

There are currently both oral and injectable protocols. The oral product usually involves capsules that must be given daily, which can be difficult for some cats and owners. The injectable product is very acidic (pH of 1.4), so SQ injection often results in wounds and significant pain to the cat. A 12-week treatment protocol, followed by observation for 12 weeks is considered the typical regimen. If there is no recurrence of clinical signs during the 12-week observation period, the patient is often considered to be cured.

Constipated Cats

I have learned to really enjoy managing constipated cats! I enjoy it because I can usually find ways for them to live very long, comfortable lives by making some simple adjustments to their daily routine.

Why do cats get constipated? Most of the cases of chronic constipation in cats are idiopathic in nature. Stress from any cause can trigger constipation in cats. The cases that I am primarily seeing are idiopathic megacolon. In the past, sub-total colectomy was the main treatment for these cats. Fortunately, in my hands, I have never had a case where I have had to even consider such a procedure.

Once I have evaluated the cat and found no other underlying disease process that needs to be addressed, my go-to diet is Royal Canin Fiber Response. I used to use W/D, years ago, but it tends to produce a larger volume of bulkier stool and I never got great results with that. The Fiber Response diet by Royal Canin is highly digestible, has a nice blend of both soluble and insoluble fiber, and it results in a more normal stool. It helps with constipation and helps with diarrhea. It doesn't result in a large volume of stool production and the stools themselves aren't typically large, so it is just easier for the cats to pass stools. The Fiber Response diet also has probiotics to help maintain good gut bacteria. It has fatty acids from fish oil and as a bonus, it has the Royal Canin S/O index to help with urinary tract health as well.

The second tool that is critical for the management of cats with constipation issues is Miralax. This is an osmotic laxative that helps keep the stools soft. It is tasteless, so it can be sprinkled on the food. Most cats will eat it without even acting like they know it's there. If they don't eat it that way, it can be mixed in their water, but I don't usually recommend this, because you really won't know how much they are getting. The recommended dose is 1/-8 -1/4 of a teaspoon per cat per day. It is available OTC. Most of my constipated cats can be managed with just those two things - Fiber Response food and daily Miralax.

For flare-ups, which may happen occasionally, lactulose is often quite effective. I typically have owners give 1 ml 2-3 times per day until a stool is produced, then keep giving that until the stools are normal to slightly soft. The official dose is 0.5 ml/kg 2-3 times per day. In many cases I think that we can prevent a hospital visit if the owners are instructed to give lactulose at the first sign of abnormal bowel movements. I don't use lactulose as the sole stool softener, because I think it can be difficult and messy to give, some cats really don't like it, and I don't think it produces the reliable stool consistency that Miralax provides. (more problems with diarrhea) Additionally, chronic administration can result in serum hypercalcemia.

Cisapride is always an additional treatment option and was widely recommended in the past. I have never really appreciated its usefulness, but the dose is 1.25-7.5 mg/cat BID-TID with food.

Of course, no treatment is perfect and many cats with constipation will still occasionally have flare-ups where they become terribly constipated and require sedation for manual evacuation of the stool. I typically sedate these cats, administer a warm water enema while sedated (5-10 mg/kg volume) and then manually remove as much stool as I can from the colon. Ideally, I keep them in the hospital on IV fluids afterwards. In many cases you can't completely evacuate the colon, so the cat will likely need to be sedated again in 1-2 days to repeat the procedure. I usually give them lactulose until the stools are being produced normally again.

Tylosin

Tylosin is a drug that has come back into favor again over the past few years. It is a macrolide antibiotic that can be helpful in the management of chronic enteropathies in dogs, particularly if intestinal dysbiosis (previously called small intestinal bacterial overgrowth) is present or suspected. This condition can be difficult to officially diagnose. It should be suspected in cases with a neutrophilic component to the enteritis on intestinal biopsies, in cases with increased folate levels on the GI panel, or in pets with excessive borborygmus and flatulence.

Who would be considered the best candidates for Tylosin? Typically, young-middle aged dogs with a history of lots of borborygmus and flatulence. It is usually used in dogs that aren't very sick, rather they just have chronic gastrointestinal problems. Tylosin could either be used before a food trial or even with the food trial. Alternatively, it could be used after they have failed a food trial. I would recommend trying Tylosin before intestinal biopsy in this scenario. If helpful, you will usually see results quickly. I like to treat twice daily for about 1 month, then try to decrease to once daily for a few months. If the pet is still doing well at that time, I try to stop it completely.

There is a pretty wide dosing range for tylosin. Most recommend 10-15 mg/kg BID or 25 mg/kg SID. The trade name is Tylan powder. Tylosin powder is very bitter tasting, so I would highly recommend having it compounded to improve compliance.

Cobalequin (Vitamin B12)

Chronic GI disease can lead to cobalamin deficiency. Additionally, sometimes low cobalamin levels can even cause chronic GI disease. One study showed that 36% of dogs with chronic GI disease had low serum cobalamin levels. This is seen specifically in some German Shepherd Dogs and is more common in cats than in dogs. Cobalamin deficiency is associated with villous atrophy and intestinal malabsorption. Signs of cobalamin deficiency could include weight loss, lethargy, and continued GI signs. In the past, B12 was thought to only be able to be absorbed parenterally, so once weekly injections were the typical protocol. More recent research has proven that cobalamin can be effectively absorbed from the intestinal tract, so it can be given as a daily oral tablet.

The recommended product is called Cobalequin, made by Nutramax. There is a tablet for cats and small dogs, as well as a larger size for medium to large breed dogs. I use this product when cobalamin deficiency is either suspected or diagnosed and use it in cases of protein-losing enteropathy.

Appetite Stimulants

In the past, the primary appetite stimulants that we had available were diazepam and cyproheptadine. Diazepam is often not recommended because it can occasionally result in fulminant liver failure if given orally. Also, it is a controlled drug, which makes administration a bit more complicated, and it causes sedation. I don't like to give my sick patients drugs that cause them to be sedate in general, because it complicates my assessment of their condition. If you use it, it does need to be given IV.

Cyproheptadine can be an effective appetite stimulant, but its effect seems to be more variable and it may take several days of administration before you see its appetite stimulating effects. It is given 1-2 times per day, 2-4 mg per cat, so sometimes just the fact that you must give a cat an oral medication so often makes it less desirable in my mind.

There are three FDA-approved products that I believe should have their place in your medicine toolbox. I don't use them a lot, and always make sure owners know that they aren't a cure-all, but they can certainly help.

Transdermal mirtazapine was one of the earlier approved appetite stimulants for cats and the beauty of it is that it is transdermal. Obviously, trying to medicate a cat who isn't eating with an oral medication is not very easy, so the transdermal route is very appealing. I have always thought that mirtazapine is helpful to stimulate appetite in cats. Additionally, it has been shown to have some anti-emetic effects. The main drawback to this medication is hyperactivity and vocalization, which are usually dose dependent. The transdermal version seems to have a more blunted appetite stimulant effect than the oral tablets, but also fewer side effects. It is typically given once daily, while the oral form is usually given every other day. The oral dose is slightly difficult to achieve - 1/8 of a 15 mg tablet per cat is the recommendation.

Entyce was the next medication that came out and it is an oral appetite stimulant for dogs. It comes in a liquid formulation, which is nice for dogs who aren't eating well. This medication works by mimicking ghrelin, which is known as the "hunger hormone". It is fairly effective in stimulating food intake. The most common side effects include diarrhea and vomiting. I tend to start low on my dosing and then increase if necessary and have not seen as much diarrhea since doing this. It is considered very safe but should be used cautiously in dogs with liver disease, because it is metabolized by the liver.

Elura was then released for use as an appetite stimulant in cats. It is the same active ingredient as Entyce, but approved for use in cats. It is an oral liquid that is vanilla flavored. I think it works somewhat well, but some of the cats that I have used it on really seem to salivate a lot when it is given.

Another little pearl that you may or may not be aware of is very low dose propofol as an appetite stimulant. It can be given IV and it is amazing how quickly and effectively it can stimulate the appetite in a dog or a cat. Usually right before they start to get sleepy, if you hold food in front of them, they will start eating pretty eagerly. The recommended dose is 2 mg/kg for a dog and 1 mg/kg for a cat. I like to use this for some of my hospitalized patients that are on IV fluids. I think it works much more reliably than the other stimulants, but obviously it can't be done at home, and it is an off-label use of the drug.

While it helps to have specialized training in Internal Medicine, there are so many things that can be done in a general practice setting! I hope that these tips and tricks today have been helpful and that you can utilize them in your own practice setting.